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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB

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 NEWS 43  Jun 06  PASCAL enhanced with additional data
 NEWS 44  Jun 20  2003 edition of the FSTA Thesaurus is now available

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 16:22:33 ON 24 JUN 2003

=> file medline, uspatful, dgene, embase, scisearch, fsta, jicst, wpids, hcaplus
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=> s lactacystin and immunosuppressive drug
L1             5 LACTACYSTIN AND IMMUNOSUPPRESSIVE DRUG

=> d l1 ti abs ibib tot

L1   ANSWER 1 OF 5  USPATFULL
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TI Synergistic method for prolonging allograft survival
AB The invention relates to allograft transplantation. More particularly, the invention relates to prolonging the survival of transplanted allografts. The invention provides a new method for improving allograft survival in a mammal. The method according to the invention provides a synergistic effect between **lactacystin** or **lactacystin** analogs and immunosuppressive drugs to prolong the survival of transplanted allografts in a mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2002:288078 USPATFULL		
TITLE:	Synergistic method for prolonging allograft survival		
INVENTOR(S):	Elliott, Peter J., Marlborough, MA, UNITED STATES Hancock, Wayne W., Philadelphia, PA, UNITED STATES		
PATENT ASSIGNEE(S):	Millennium Pharmaceuticals, Inc., Cambridge, MA (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002160947	A1	20021031
APPLICATION INFO.:	US 2002-114602	A1	20020402 (10)
	NUMBER		DATE
PRIORITY INFORMATION:	US 2001-281088P		20010403 (60)
	US 2001-282535P		20010409 (60)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	HALE AND DORR, LLP, 60 STATE STREET, BOSTON, MA, 02109		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Page(s)		
LINE COUNT:	274		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 2 OF 5 USPATFULL
TI Use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock
AB The present invention relates to compositions comprising proteasome inhibitors, such as **lactacystin**, DPBA and their analogs. These compositions are used for the following purposes: (1) to disrupt mitochondrial function (useful aganst cancer, inflammation, adverse immune reaction and hyperthyroidism), (2) to disrupt nitric oxide synthesis (useful against inflammation and septic shock), and (3) to reverse ongoing adverse immune reactions, such as autoimmune diseases and graft rejection. In the later case, the compositions can be administered once the patients' T cells are mostly activated. Proteasome inhibitors can also be combined to immuno-suppressinve drugs like rapamycin, cyclosporin A and FK506. Finally, a method for screening a compound having a proteasome inhibition activity is also disclosed and claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2002:92633 USPATFULL		
TITLE:	Use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock		
INVENTOR(S):	Wu, Jiangping, Brossard, CANADA Wang, Xin, Montreal, CANADA		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002049157	A1	20020425
APPLICATION INFO.:	US 2001-904251	A1	20010712 (9)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1999-341009, filed on 25 Aug 1999, PENDING A 371 of International Ser. No. WO 1998-CA1010, filed on 29 Oct 1998, UNKNOWN	
	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-218145P	20000714 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	34 Drawing Page(s)	
LINE COUNT:	2010	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 3 OF 5 SCISEARCH COPYRIGHT 2003 THOMSON ISI

TI Rapamycin inhibits proteasome activator expression and proteasome activity

AB Rapamycin (RAPA) is a potent **immunosuppressive drug** , and certain of its direct or indirect targets might be of vital importance to the regulation of an immune response. In this study, we used differential hybridization to search for human genes whose expression was sensitive to RAPA. Seven RAPA-sensitive genes were found and one of them encoded a protein with high homology to the ct subunit of a proteasome activator (PA28 beta). This gene was later found to code for the IJ subunit of the proteasome activator (PA28 beta). Activated T and B cells had up-regulated PA28 beta expression at the mRNA level. Such up-regulation could be suppressed by RAPA, FK506, and cyclosporin A. RAPA and FK506 also repressed the up-regulated PA28 alpha messages in phytohemagglutinin (PHA) stimulated T cells. At the protein level, RAPA inhibited PA28 alpha and PA28 beta in the activated T cells according to immunoblotting and confocal microscopy. Probably as a consequence, there was a fourfold increase of proteasome activities in the peripheral blood mononuclear cell lysate after the PHA activation. RAPA could inhibit the enhanced part of the proteasome activity. Considering the critical role played by the proteasome in degrading regulatory proteins, our data suggest that the proteasome activator is a relevant and important downstream target of rapamycin, and that the immune response could be modulated through the activity of the proteasome.

ACCESSION NUMBER: 97:865944 SCISEARCH
THE GENUINE ARTICLE: YG422

TITLE: Rapamycin inhibits proteasome activator expression and proteasome activity

AUTHOR: Wang X; Omura S; Szweda L I; Yang Y; Berard J; Seminaro J; Wu J P (Reprint)

CORPORATE SOURCE: UNIV MONTREAL, NOTRE DAME HOSP, LC SIMARD RES CTR, PAVIL DE SEVE Y-5616, 1560 SHERBROOKE ST E, MONTREAL, PQ H2L 4M1, CANADA (Reprint); UNIV MONTREAL, FAC MED, LOUIS CHARLES SIMARD RES CTR, LAB TRANSPLANTAT IMMUNOL, DEPT MED, MONTREAL, PQ H3C 3J7, CANADA; UNIV MONTREAL, FAC MED, DEPT MED, SERV NEPHROL, MONTREAL, PQ H3C 3J7, CANADA; KITASATO INST, TOKYO 108, JAPAN; CASE WESTERN RESERVE UNIV, CLEVELAND, OH 44106; RW JOHNSON PHARMACEUT RES INST, SAN DIEGO, CA 92121; UNIV SHERBROOKE, SHERBROOKE, PQ J1K 2R1, CANADA; MCGILL UNIV, DEPT SURG, MONTREAL, PQ H3A 2T5, CANADA

COUNTRY OF AUTHOR: CANADA; JAPAN; USA

SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (NOV 1997) Vol. 27, No. 11, pp. 2781-2786.
Publisher: VCH PUBLISHERS INC, 303 NW 12TH AVE, DEERFIELD BEACH, FL 33442-1788.
ISSN: 0014-2980.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 40
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L1 ANSWER 4 OF 5 WPIDS (C) 2003 THOMSON DERWENT
TI Use of a proteasome inhibitor for reversing proliferation or activity of activated blood cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.
AN 2002-507279 [54] WPIDS
CR 1999-313169 [26]
AB US2002049157 A UPAB: 20020823
NOVELTY - A novel method for reversing an ongoing proliferation or activity, or both, of activated blood cells, comprises administering a proteasome inhibitor to an individual.

ACTIVITY - Immunosuppressive; Antiinflammatory; Antibacterial; Cytostatic.

MECHANISM OF ACTION - Proteasome inhibitor; inhibitors of CDK2 and Cyclin E.

The role of proteasome in T cell activation and proliferation was first examined in PBMC, using the proteasome-specific inhibitor LAC. The peripheral blood mononuclear cells (PBMC) were activated with various stimulants. LAC was added to the cells in the beginning of the culture (0 hours) along with the stimulants. 3H-thymidine uptake between 48 and 64 hours of 64 hour cultures was used as a parameter for cell proliferation. LAC strongly and dose-dependently inhibited the T cell proliferation induced by a T cell mitogen PHA by crosslinking TCR with anti-CD3 E, or by Ca++ ionophore plus cross-linking of the T cell co-stimulating molecule CD28. The T-cell-independent B cell proliferation induced with SAC plus IL-2 in tonsillar B cells was also potently inhibited by LAC. In all systems used, LAC at 5 micro M could exert near-to-maximal inhibition. The results suggest that LACs effect is not lymphocyte type (T or B cells)-specific nor stimulant-specific. It likely affects certain down-stream events governing a more general process in lymphocyte activation and proliferation.

USE - The methods can be used for treating an adverse immune response such as an autoimmune disease or a graft rejection, or inflammation or septic shock (claimed). The methods can be used for reversing an ongoing proliferation or activity which may result in activated blood cells apoptosis, or inhibition of energy and oxygen supply to the activated blood cells, or where the inhibition of energy and oxygen supply is caused by disrupting mitochondrial function in activated blood cells or disruption of nitric acid synthesis (claimed). The methods can also be used for treating e.g. cancers, hyperthyroidisn and graft rejection.

The use of DPBA in organ transplantation-islet graft in streptozocin-induced diabetes in mice was studied. Islets from Balb/c mice in diabetic C57BL/6 recipients were used. The islets from syngeneic mice (isograft control) restored normal glycemia in diabetic mice, and the effect lasted more than 60 days as expected. The allogenic islets were rejected in about 10 days in untreated mice, and the mice became diabetic after an initial dip of their blood sugar level (allograft control). When the allogenic islets were transplanted to diabetic recipients along with DPBA treatment, the graft functioned normally beyond 60 days, indicating that the graft rejection was inhibited. This result showed that proteasome inhibitors as exemplified by DPBA can be used in human islet transplantation to prevent graft rejection. It was shown that a proteasome inhibitor such as DPBA inhibits the glucose elevation consequent to islet rejection.

ADVANTAGE - The proteasome inhibitors such as LAC and DPBA have shown an unique capacity to reverse an ongoing activity of blood cells. This reversal makes the possibility of treatment which selectively targets activated blood cells. The protease inhibitor are responsible for preventing allograft rejection for the first time successfully. Also an effective screening method for searching for other proteasome inhibitors

has been found.
Dwg.0/31

ACCESSION NUMBER: 2002-507279 [54] WPIDS
CROSS REFERENCE: 1999-313169 [26]
DOC. NO. CPI: C2002-144189
TITLE: Use of a proteasome inhibitor for reversing proliferation or activity of activated blood cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.
DERWENT CLASS: B04 B05
INVENTOR(S): WANG, X; WU, J
PATENT ASSIGNEE(S): (WANG-I) WANG X; (WUJJ-I) WU J
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002049157	A1	20020425	(200254)*		54

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002049157	A1 CIP of	WO 1998-CA1010	19981029
	CIP of	US 1999-341009	19990825
	Provisional	US 2000-218145P	20000714
		US 2001-904251	20010712

PRIORITY APPLN. INFO: US 2000-218145P 20000714; WO 1998-CA1010 19981029; US 1999-341009 19990825; US 2001-904251 20010712

L1 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS
TI Combination of **lactacystin** analog and **immunosuppressive drug** for the prolongation of allograft survival
AB The invention relates to allograft transplantation. More particularly, the invention relates to prolonging the survival of transplanted allografts. The invention provides a new method for improving allograft survival in a mammal. The method according to the invention provides a synergistic effect between **lactacystin** or **lactacystin** analogs and immunosuppressive drugs to prolong the survival of transplanted allografts in a mammal.
ACCESSION NUMBER: 2002:793409 HCAPLUS
DOCUMENT NUMBER: 137:288996
TITLE: Combination of **lactacystin** analog and **immunosuppressive drug** for the prolongation of allograft survival
INVENTOR(S): Hancock, Wayne W.; Elliott, Peter J.
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080907	A1	20021017	WO 2002-US10278	20020402

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002160947 A1 20021031 US 2002-114602 20020402
PRIORITY APPLN. INFO.: US 2001-281088P P 20010403
US 2001-282535P P 20010409
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s PHA
L2 52589 PHA

=> d his

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FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, SCISEARCH, FSTA, JICST-EPLUS, WPIDS, HCAPLUS' ENTERED AT 16:26:35 ON 24 JUN 2003
L1 5 S LACTACYSTIN AND IMMUNOSUPPRESSIVE DRUG
L2 52589 S PHA

=> s l1 and l2
L3 3 L1 AND L2

=> d l3 ti abs ibib tot

L3 ANSWER 1 OF 3 USPATFULL
TI Use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock
AB The present invention relates to compositions comprising proteasome inhibitors, such as **lactacystin**, DPBA and their analogs. These compositions are used for the following purposes: (1) to disrupt mitochondrial function (useful aganst cancer, inflammation, adverse immune reaction and hyperthyroidism), (2) to disrupt nitric oxide synthesis (useful against inflammation and septic shock), and (3) to reverse ongoing adverse immune reactions, such as autoimmune diseases and graft rejection. In the later case, the compositions can be administered once the patients' T cells are mostly activated. Proteasome inhibitors can also be combined to immuno-suppressinve drugs like rapamycin, cyclosporin A and FK506. Finally, a method for screening a compound having a proteasome inhibition activity is also disclosed and claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:92633 USPATFULL
TITLE: Use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock
INVENTOR(S): Wu, Jiangping, Brossard, CANADA
Wang, Xin, Montreal, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002049157	A1	20020425
APPLICATION INFO.:	US 2001-904251	A1	20010712 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-341009, filed on 25 Aug 1999, PENDING A 371 of International Ser. No. WO 1998-CA1010, filed on 29 Oct 1998, UNKNOWN

NUMBER	DATE

PRIORITY INFORMATION: US 2000-218145P 20000714 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 2010
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 2 OF 3 SCISEARCH COPYRIGHT 2003 THOMSON ISI
TI Rapamycin inhibits proteasome activator expression and proteasome activity
AB Rapamycin (RAPA) is a potent **immunosuppressive drug**, and certain of its direct or indirect targets might be of vital importance to the regulation of an immune response. In this study, we used differential hybridization to search for human genes whose expression was sensitive to RAPA. Seven RAPA-sensitive genes were found and one of them encoded a protein with high homology to the ct subunit of a proteasome activator (PA28 beta). This gene was later found to code for the IJ subunit of the proteasome activator (PA28 beta). Activated T and B cells had up-regulated PA28 beta expression at the mRNA level. Such up-regulation could be suppressed by RAPA, FK506, and cyclosporin A. RAPA and FK506 also repressed the up-regulated PA28 alpha messages in phytohemagglutinin (**PHA**) stimulated T cells. At the protein level, RAPA inhibited PA28 alpha and PA28 beta in the activated T cells according to immunoblotting and confocal microscopy. Probably as a consequence, there was a fourfold increase of proteasome activities in the peripheral blood mononuclear cell lysate after the **PHA** activation. RAPA could inhibit the enhanced part of the proteasome activity. Considering the critical role played by the proteasome in degrading regulatory proteins, our data suggest that the proteasome activator is a relevant and important downstream target of rapamycin, and that the immune response could be modulated through the activity of the proteasome.
ACCESSION NUMBER: 97:865944 SCISEARCH
THE GENUINE ARTICLE: YG422
TITLE: Rapamycin inhibits proteasome activator expression and proteasome activity
AUTHOR: Wang X; Omura S; Szweda L I; Yang Y; Berard J; Seminaro J; Wu J P (Reprint)
CORPORATE SOURCE: UNIV MONTREAL, NOTRE DAME HOSP, LC SIMARD RES CTR, PAVIL DE SEVE Y-5616, 1560 SHERBROOKE ST E, MONTREAL, PQ H2L 4M1, CANADA (Reprint); UNIV MONTREAL, FAC MED, LOUIS CHARLES SIMARD RES CTR, LAB TRANSPLANTAT IMMUNOL, DEPT MED, MONTREAL, PQ H3C 3J7, CANADA; UNIV MONTREAL, FAC MED, DEPT MED, SERV NEPHROL, MONTREAL, PQ H3C 3J7, CANADA; KITASATO INST, TOKYO 108, JAPAN; CASE WESTERN RESERVE UNIV, CLEVELAND, OH 44106; RW JOHNSON PHARMACEUT RES INST, SAN DIEGO, CA 92121; UNIV SHERBROOKE, SHERBROOKE, PQ J1K 2R1, CANADA; MCGILL UNIV, DEPT SURG, MONTREAL, PQ H3A 2T5, CANADA
COUNTRY OF AUTHOR: CANADA; JAPAN; USA
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (NOV 1997) Vol. 27, No. 11, pp. 2781-2786.
Publisher: VCH PUBLISHERS INC, 303 NW 12TH AVE, DEERFIELD BEACH, FL 33442-1788.
ISSN: 0014-2980.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 40
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L3 ANSWER 3 OF 3 WPIDS (C) 2003 THOMSON DERWENT
TI Use of a proteasome inhibitor for reversing proliferation or activity of activated blood cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.
AN 2002-507279 [54] WPIDS
CR 1999-313169 [26]
AB US2002049157 A UPAB: 20020823
NOVELTY - A novel method for reversing an ongoing proliferation or activity, or both, of activated blood cells, comprises administering a proteasome inhibitor to an individual.

ACTIVITY - Immunosuppressive; Antiinflammatory; Antibacterial; Cytostatic.

MECHANISM OF ACTION - Proteasome inhibitor; inhibitors of CDK2 and Cyclin E.

The role of proteasome in T cell activation and proliferation was first examined in PBMC, using the proteasome-specific inhibitor LAC. The peripheral blood mononuclear cells (PBMC) were activated with various stimulants. LAC was added to the cells in the beginning of the culture (0 hours) along with the stimulants. 3H-thymidine uptake between 48 and 64 hours of 64 hour cultures was used as a parameter for cell proliferation. LAC strongly and dose-dependently inhibited the T cell proliferation induced by a T cell mitogen **PHA** by crosslinking TCR with anti-CD3 E, or by Ca++ ionophore plus cross-linking of the T cell co-stimulating molecule CD28. The T-cell-independent B cell proliferation induced with SAC plus IL-2 in tonsillar B cells was also potently inhibited by LAC. In all systems used, LAC at 5 micro M could exert near-to-maximal inhibition. The results suggest that LACs effect is not lymphocyte type (T or B cells)-specific nor stimulant-specific. It likely affects certain down-stream events governing a more general process in lymphocyte activation and proliferation.

USE - The methods can be used for treating an adverse immune response such as an autoimmune disease or a graft rejection, or inflammation or septic shock (claimed). The methods can be used for reversing an ongoing proliferation or activity which may result in activated blood cells apoptosis, or inhibition of energy and oxygen supply to the activated blood cells, or where the inhibition of energy and oxygen supply is caused by disrupting mitochondrial function in activated blood cells or disruption of nitric acid synthesis (claimed). The methods can also be used for treating e.g. cancers, hyperthyroidisn and graft rejection.

The use of DPBA in organ transplantation-islet graft in streptozocin-induced diabetes in mice was studied. Islets from Balb/c mice in diabetic C57BL/6 recipients were used. The islets from syngeneic mice (isograft control) restored normal glycemia in diabetic mice, and the effect lasted more than 60 days as expected. The allogenic islets were rejected in about 10 days in untreated mice, and the mice became diabetic after an initial dip of their blood sugar level (allograft control). When the allogenic islets were transplanted to diabetic recipients along with DPBA treatment, the graft functioned normally beyond 60 days, indicating that the graft rejection was inhibited. This result showed that proteasome inhibitors as exemplified by DPBA can be used in human islet transplantation to prevent graft rejection. It was shown that a proteasome inhibitor such as DPBA inhibits the glucose elevation consequent to islet rejection.

ADVANTAGE - The proteasome inhibitors such as LAC and DPBA have shown an unique capacity to reverse an ongoing activity of blood cells. This reversal makes the possibility of treatment which selectively targets activated blood cells. The protease inhibitor are responsible for preventing allograft rejection for the first time successfully. Also an effective screening method for searching for other proteasome inhibitors has been found.

Dwg.0/31

ACCESSION NUMBER: 2002-507279 [54] WPIDS
CROSS REFERENCE: 1999-313169 [26]
DOC. NO. CPI: C2002-144189

TITLE: Use of a proteasome inhibitor for reversing proliferation or activity of activated blood cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.
DERWENT CLASS: B04 B05
INVENTOR(S): WANG, X; WU, J
PATENT ASSIGNEE(S): (WANG-I) WANG X; (WUJJ-I) WU J
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002049157	A1	20020425	(200254)*		54

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2002049157	A1	CIP of	WO 1998-CA1010	19981029
		CIP of	US 1999-341009	19990825
		Provisional	US 2000-218145P	20000714
			US 2001-904251	20010712

PRIORITY APPLN. INFO: US 2000-218145P 20000714; WO 1998-CA1010 19981029; US 1999-341009 19990825; US 2001-904251 20010712

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(FILE 'HOME' ENTERED AT 16:22:33 ON 24 JUN 2003)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, SCISEARCH, FSTA, JICST-EPLUS, WPIDS, HCAPLUS' ENTERED AT 16:26:35 ON 24 JUN 2003

```
L1             5 S LACTACYSTIN AND IMMUNOSUPPRESSIVE DRUG
L2         52589 S PHA
L3             3 S L1 AND L2
```

=> e Wu, J/au

```
E1            87     WU ZUZE/AU
E2             1     WU ZUZU/AU
E3             0 --> WU, J/AU
E4             1     WUA H H/AU
E5             1     WUADE U/AU
E6             1     WUAGH D/AU
E7             2     WUAGNEUX D/AU
E8             1     WUAHOUJU G/AU
E9             1     WUAK M/AU
E10            1     WUALMANN H/AU
E11            8     WUAMETT J D/AU
E12            1     WUAN G Y/AU
```

=> e wang, X/au

```
E1             1     WANG ZXINGTAI/AU
E2             2     WANG ZYX/AU
E3             0 --> WANG, X/AU
E4             1     WANG1 Y/AU
E5             1     WANGA A P/AU
E6             1     WANGA C/AU
E7             1     WANGA C C/AU
E8             1     WANGA D/AU
E9             1     WANGA D B/AU
E10            1     WANGA G/AU
```

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E11          1     WANGA G J/AU
E12          1     WANGA I/AU

=> s e1
L4           1 "WANG ZXINGTAI"/AU

=> d l4 ti abs ibib tot

L4   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2003 ACS
TI   Application of synthetic peptides in detection of antibody to hepatitis G
     virus
AB   According to the hepatitis G virus (HGV) protein amino acid sequences, 4
     peptides from different regions were selected based on computer anal. of
     the hydrophility and antigenic epitopes and were synthesized by the
     conventional solid phase method.  With the synthetic peptides, an indirect
     ELISA was developed to detect anti-HGV IgG.  Among 57 sera from non A-3
     hepatitis patients, 20 were pos. for anti-HGV IgG, the pos. rate was
     35.09% (20/57), 14 were pos. for HGV RNA, the pos. rate was 24.56%
     (14/57).  We also tested 30 sera from hepatitis A patients, 10 from
     hepatitis B and 46 form hepatitis C, and the pos. rates for anti-HGV IgG
     were 3.33%, 10% and 8.70% resp.  The coinfection rate is relatively high
     in viral hepatitis patients in China.  Therefore HGV infection should be
     given attention to in the differential diagnosis of hepatitis.
ACCESSION NUMBER:        1997:418088  HCAPLUS
DOCUMENT NUMBER:         127:107679
TITLE:                   Application of synthetic peptides in detection of
                         antibody to hepatitis G virus
AUTHOR(S):               Mao, Panyong, Hong, Shiwen; Hong, Shiwen; He, Hongxia;
                         Hu, Yan; Wang, zXingtai; Zhu, Chuanlin; Lou,
                         Min; Liang, Yong; Yang, Jianyang; Ju, Liancai; Bai,
                         Yanping
CORPORATE SOURCE:        Dep. Virol., PLA Hosp., Beijing, 10039, Peop. Rep.
                         China
SOURCE:                  Zhonghua Shiyan He Linchuang Bingduxue Zazhi (1996),
                         10(4), 371-373
                         CODEN: ZSLZFS; ISSN: 1003-9279
PUBLISHER:               Weishengbu Wuhan Shengwu Zhipin Yanjiuso
DOCUMENT TYPE:           Journal
LANGUAGE:                Chinese


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L2       52589 S PHA
L3           3 S L1 AND L2
               E WU, J/AU
               E WANG, X/AU
L4           1 S E1
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